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Paucidactine A and B, New Indole Alkaloids with a Novel Ring System containing a Lactone Moiety

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Abstract *: Two new indole alkaloids viz., Paucidactine A and B, possessing a novel heptacyclic carbon skeleton incorporating a lactone unit were obtained from Kopsia pauciflora. The structures of these alkaloids were elucidated by 2-D NMR methods and confirmed by X-ray analysis.*

The genus *Kopsia* which has its stronghold in Southeast Asia, has proven to be a fertile source of structurally novel alkaloids[1-4]. In continuation of our studies of the Malaysian genus[1], we investigated the alkaloidal composition of *Kopsia pauciflora* Hook f., a species found in North Borneo[2] and wish to report a novel class of indoles exemplified by paucidactine A and B (**1** & **2**). These indole alkaloids possess a novel carbon skeleton incorporating a six-membered lactone ring as part of the heptacyclic ring system.

Paucidactine A was obtained as light yellow crystals, mp 279-280°, $[\alpha]_D$ + 53.8° ($CHCl_3$, *c* 0.156). The EIMS of paucidactine A **1**[5] showed a molecular ion at *m/z* 470 ($C_{23}H_{22}N_2O_9$, 100 %) with other significant fragments at 442 (M - $CH_2{=}CH_2$), 426 (M - CO_2) and 412 (M - CO_2Me + H). The UV spectrum showed absorption maxima at 225, 244, 286 and 290 nm which indicate the presence of a dihydroindole chromophore. The ^1H and ^{13}C NMR spectral data (Table 1) showed the presence of a methylenedioxy substituent at carbon-11 and 12 (a pair of aromatic AB doublets at δ_H 6.64 & 6.77 and another pair at δ_H 6.00, 5.95, δ_C 101.1), a CO_2Me substituent at N_1 (δ_C 153.8), 2 hydroxyl groups (16-OH, δ_H 6.65; 21-OH δ_H 3.33), a lactam carbonyl at carbon-5 (δ_C 165.7) and a lactone carbonyl function (δ_C 169.3). Two oxygenated quaternary carbons are indicated by the carbon resonances at δ_C 74.1 (C-16) and δ_C 88.6 (C-21). A conspicuous feature of the ^1H NMR spectrum is the presence of a low field single H singlet at δ 4.74 which is attributed to H-6 (*vide infra*). COSY and HMQC experiments revealed the presence of the following partial structures, *viz.*, an isolated methylene group, an isolated oxymethine, a CH_2-CH_2 unit and a CH_2-CH_2-CH_2 fragment. This information suggest that the lactam carbonyl should be placed at position 5 since the alternative location of the lactam carbonyl at position 3 would result in two CH_2-CH_2 fragments which was not the case.

This would also be in accord with the observed carbon resonance of C-6 at δ_C 84.0 since it is α to both an oxygen and a carbonyl function. It would also account for the unusual deshielding observed for H-3β (δ_H 4.04) as a result of the anisotropy due to the proximate lactam carbonyl function. Of the two hydroxyl groups one is placed at C-16 since the observed NMR chemical shifts are typical of α-OH groups on carbon-16 in related aspidofractinine-type alkaloids[1d] and furthermore this can be confirmed from the observed ^3J (C-17 to 16-OH) and ^2J (C-16 to 16-OH) interactions in HMBC. The presence of another hydroxyl group on C-21 is indicated by the absence of signals normally attributable to H-21 (*c.f.* compound **2**), the presence of an OH signal at δ_H 3.33, as well as the observed ^3J correlation between C-20 and 21-OH in HMBC. These and other correlations from HMBC experiments enabled the molecule to be assembled as shown in **1** in which C-16 and C-6 are now linked by a lactone function (^3J , C-22 to H-6). The formation of the additional 6-membered lactone ring unit as part of the overall heptacyclic indole ring system constitutes the unique feature of this new class of indole alkaloid. The related compound, paucidactine B **2**[6] was the minor alkaloid isolated compared to **1** and resembles paucidactine A **1** in all respects except that the 21-OH is now absent, being replaced by a hydrogen (δ_H 3.64). The 21-hydrogen being α, experiences long range *W* coupling with H-17α (2 Hz) which was also confirmed from the COSY spectrum. Since paucidactine A **1** yielded well formed crystals, we thought it prudent to confirm the structure by X-ray analysis[7]. The crystals of paucidactine **1** are orthorhombic, belonging to space group $P2_12_12_1$, with a = 13.4708(4), b = 29.1176(10), c = 10.1782(4) Å, $\alpha = \beta = \gamma = 90^0$, V = 3992.3(2) Å^3, D_x = 1.565 Mg m^{-3} and Z = 8. The structure was solved by direct methods and refined by the least squares method. The final R-factor was 0.1109. The results are shown in the perspective view in Figure 1, which provides vindication of our conclusions deduced from spectral data above.

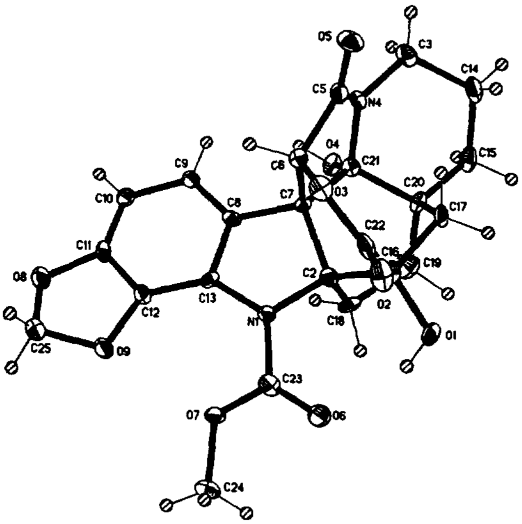
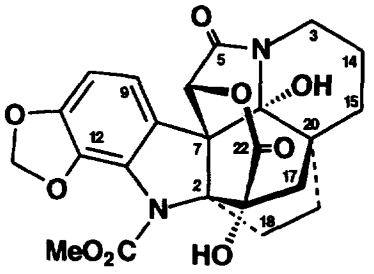
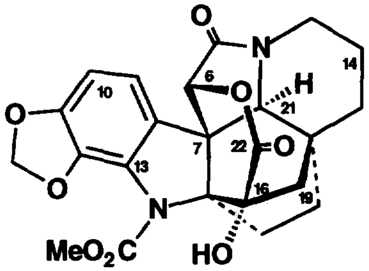


Fig. 1 Perspective view of paucidactine A



1



2

Table 1. ^{1}H and ^{13}C NMR Spectral Data for **1** and **2**[a]

	1		**2**	
Position	δ_C	δ_H	δ_C	δ_H
2	71.3	-	71.0	-
3α	37.9	3.15 td (13, 3.5)	40.6	2.85 td (13, 4)
3β	-	4.04 dd (13, 5.5)	-	4.28 m
5	165.7	-	166.9	-
6	84.0	4.74 s	83.3	4.62 s
7	53.3	-	48.7	-
8	126.2	-	129.8	-
9	115.9	6.77 d (7.8)	114.3	6.62 m
10	105.2	6.64 d (7.8)	105.1	6.62 m
11	150.3	-	150.1	-
12	136.3	-	136.2	-
13	124.0	-	123.0	-
14a	20.9	1.54 m	19.7	1.59 m
14b	-	1.61 m	-	1.59 m
15a	29.3	1.49 m	33.5	1.45 m
15b	-	1.95 td (13, 4.5)	-	1.73 m
16	74.1	-	74.0	-
17α	42.0	1.68 m	39.4	1.69 m
17β	-	2.29 br d (15.6)	-	2.33 br d (15.6)
18a	20.9	1.74 m	21.0	1.67 m
18b	-	2.40 m	-	2.46 ddd (13.5, 11, 2)
19a	26.9	1.76 m	29.7	1.38 m
19b	-	1.80 m	-	1.97 td (12.5, 7.5)
20	37.0	-	33.7	-
21	88.6	-	64.5	3.64 d(2)
22	169.3	-	169.4	-
OCH$_2$O	101.1	5.95 d (1.5); 6.00 d (1.5)	101.1	5.99 d (1.5); 5.95 d (1.5)
NCO$_2\underline{\text{Me}}$	53.8	3.83 s	53.8	3.83 s
N$\underline{\text{C}}$O$_2$Me	153.8	-	153.8	-
16-OH	-	6.65 s	-	6.55 s
21-OH	-	3.33 s	-	-

[a] CDCl$_3$, 270 MHz; assignments based on COSY, HMQC and HMBC.

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5. Compound **1**, Paucidactine A, EIMS, *m/z* (rel. int.) : 470 [M^+] (100), 454 (5), 442 (3), 426 (40), 409 (15), 398 (7), 367 (6), 341 (7) and 300 (5). HREIMS, M^+ found 470.1329, calcd. for $C_{23}H_{22}N_2O_9$ 470.1325. UV (EtOH), λ_{max} (log ε) 225 (4.74), 244 (4.25), 286 (3.47) and 290 (3.45). $[\alpha]_D = 53.8^o$ ($CHCl_3$, c = 0.156). ^1H and ^{13}C NMR : see Table 1.
6. Compound **2**, Paucidactine B, EIMS, *m/z* (rel. int.) : 454 [M^+] (100), 440 (10), 426 (10), 410 (90), 396 (12), 382 (15), 369 (14), 351 (10), 339 (10), 323 (12) and 309 (9). HREIMS, M^+ found 454.1379, calcd. for $C_{23}H_{22}N_2O_8$ 454.1376. UV (EtOH), λ_{max} (log ε) 225 (4.47), 245 (3.94), 288 (3.06) and 292 (3.06). $[\alpha]_D = 1.2^o$ ($CHCl_3$, c = 0.017). ^1H and ^{13}C NMR : see Table 1.
7. Full crystal data for **1** are deposited at the Cambridge Crystallographic Data Center.

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